

CLAIMS:

1. A method for delivering a pharmaceutical polypeptide agent through a body surface, comprising:

5 (a) providing a synthetic analog of a pharmaceutical parent polypeptide agent, said analog having at least one amino acid residue of the parent polypeptide agent substituted by a histidine residue (His); and

(b) delivering the analog through the body surface by electrotransport.

10 2. The method of claim 1, wherein the residue of the parent polypeptide agent is selected from the group consisting of glutamine (Gln), threonine (Thr) and asparagine (Asn).

15 3. The method of claim 1, wherein the residue of the parent polypeptide agent comprises glutamine (Gln).

4. The method of claim 1, wherein the analog exhibits at least about the same biological activity as the parent polypeptide agent.

20 5. A method of modifying a pharmaceutical polypeptide agent to enhance electrotransport through a body surface, comprising:

substituting a histidine residue for one or more glutamine residues of the parent pharmaceutical polypeptide agent to form a synthetic analog of the parent agent, said analog having greater the overall charge than the charge on the parent agent at a pH of about 3.5-8.

25 6. A synthetic analog of a parent polypeptide, which parent polypeptide has at least one amino acid residue that has a polar but uncharged side chain, said analog having at least one of said residues substituted by a histidine residue.

7. The analog of claim 6, said analog exhibiting a biological activity at least about the same as the parent polypeptide.

5 8. The analog of claim 6, wherein said amino acid residue that has a polar but uncharged side chain is selected from the group consisting of glutamine, asparagine and threonine.

10 9. The analog of claim 8, wherein said amino acid residue having a polar but uncharged side chain is glutamine.

15 10. A pharmaceutical composition comprising a therapeutically effective amount of the analog of claims 6, 7, 8, or 9 and acceptable physiological carriers or excipients therefor.

20 11. A synthetic analog having enhanced electrotransport activity through a body surface of a parent pharmaceutical polypeptide agent, which parent has at least one residue selected from the group consisting of glutamine, threonine and asparagine, said analog having at least one of said residues substituted by a histidine residue.

12. The analog of claim 11, the analog exhibiting a biological activity at least about the same as the parent polypeptide.

13. The analog of claim 11, wherein every Gln residue in the parent polypeptide is substituted by His in the analog.

20 14. The analog of claim 11, wherein the overall charge of said analog is positive at a pH in the range of about 5 to 6 but substantially isoelectric at pH 7.4.

15. The analog of claim 11, wherein said analog has a greater positive charge at a pH in the range of about 5 to 6 than the parent polypeptide.

16. A composition comprising a pharmaceutical polypeptide agent modified to have at least one glutamine residue substituted by a histidine residue to form an analog wherein the analog has a greater overall charge than the charge on the agent at a pH of about 5-6 and enhances the electrotransport delivery of the agent.

add
Art